and may provide an alternative to surgery in symptomatic patients with HOCM. Longer-term follow-up in larger numbers of patients are awaited.

977-121 Clinical Significance of LV "Aftercontraction" and "Contraction Dispersion" by Doppler Tissue Imaging

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Asynchrony in LV relaxation is known to impair global LV function and its filling. We investigated the dynamics of LV long axis shortening using pulsed wave Doppler tissue imaging in 44 subjects: 10 with normal cardiac anatomy (NL), 17 with LV hypertrophy and 17 with semental wall motion abnormalities (WMA). Spectral velocities profiles from medial, lateral, anterior and posterior portions of the mitral annulus were recorded from the apical view; their peak velocities, durations, and timing to R wave of the ECG and LV ejection were measured. Presence of apical motion of the annulus after the end of ejection was referred to as LV aftercontraction and the difference between longest and shortest durations of the systolic velocities as contraction dispersion.

Results: Incidence of aftercontraction was 1/10 in NL, 12/17 in LVH ($p < 0.01$ vs NL) and 8/17 in WMA ($p < 0.05$ vs NL) groups. The durations of apically directed systolic velocities were similar in all 3 groups, but the amplitudes and time velocity integrals were reduced in LVH and WMA. The timing of these velocities in relation to the R wave of the ECG were marginally prolonged in those with LVH. The contraction dispersion was 40 ± 23 msec in NL, 53 ± 23 msec in LVH and 45 ± 24 msec in WMA ($p = 0.06$). The transmitral A wave amplitude, but not the A/E velocity ratio or the LV isovolumic relaxation time was significantly greater in those with aftercontractions.

Conclusions: 1. Amplitudes and timings of the regional mitral annular velocities are affected by LVH and WMA. 2. LV aftercontractions are present in LVH and WMA. 3. LV contraction dispersion which is a measure of asynchronous LV contraction is increased in LVH.

977-122 Biopsy-Proven Eosinophilic Endomyocardial Disease: Survival Analysis of 25 Patients

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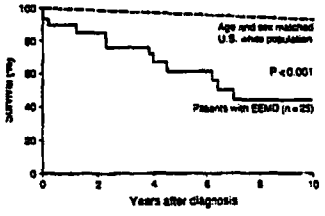
Eosinophilic endomyocardial disease (EEMD) is a rarely recognized myocarditis with clinical characteristics that have not been well described. We reviewed our experience with biopsy-proven EEMD, including survival analysis. Biopsy diagnosis was aided by a specific immunofluorescence antibody method for major basic protein, a cytotoxic protein by-product of eosinophil degranulation. We identified 26 pts (14 M; 12F) with biopsy-proven EEMD diagnosed between 1980 and 1994. Pt age ranged from 8–75 yrs (mean 48 ± 20). EEMD was associated with peripheral eosinophilia due to idiopathic hypereosinophilic syndrome (HES) (n = 10), atopy (n = 7), Churg-Strauss syndrome (n = 2), hypersensitivity (n = 2), or unknown (n = 1). Four pts did not have peripheral eosinophilia. Mean LVEF at diagnosis was 50 ± 19%. Twenty-one of 25 pts were treated with immunosuppression comprised of hydroxyurea and/or corticosteroids Morbidity was predominantly due to cardiac disease; 22 of 26 pts presented with cardiovascular symptoms. Kaplan-Meier survival analysis was performed for 25 of 26 pts (one pt lost to follow-up). Mean follow-up duration was 5.3 ± 4.0 yrs. Five and 10 yr survival was 60% and 42%, respectively, significantly less than an age- and gender-matched control population. Patients with HES tended to have better survival than 15 pts with EEMD due to other causes, but the difference did not reach statistical significance ($p = 0.09$).



Conclusion: Biopsy-proven EEMD is associated with a poor prognosis despite immunosuppression. Pts with EEMD due to HES may have a better prognosis than pts with EEMD due to other causes.

978 Neurohormonal Factors in Heart Failure

Tuesday, March 26, 1996, 3:00 p.m.–5:00 p.m.
Orange County Convention Center, Hall E
Presentation Hour: 4:00 p.m.–5:00 p.m.

978-93 Dual Inhibition of Neutral Endopeptidase and Angiotensin Converting Enzyme Delays the Progression of Experimental Heart Failure

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The syndrome of overt congestive heart failure (CHF) represents a state of cardiorenal decompensation with humoral activation, vasoconstriction, sodium retention, and ventricular remodeling. In a canine model of CHF produced by incremental pacing over 4 weeks, with early and sustained activation of natriuretic peptides and stimulation of vasoconstrictive factors, sodium retention and increased left ventricular mass (LVM) we tested the hypothesis that potentiation of the vasodilatory natriuretic peptide system (NPS) and attenuation of the renin-angiotensin-aldosterone system (RAAS) with combined neutral endopeptidase (NEPI) and angiotensin-converting enzyme inhibition (ACEI) (UK81252, Pfizer, 10 mg/kg, po bid) would improve cardiorenal hemodynamics, sodium excretion, and decrease LVM. Compared to control dogs (n = 8), UK dogs (n = 6) had a greater decrease in MAP (Δ −36 ± 4 vs −14 ± 2 mmHg*) and less increase in systemic vascular resistance (Δ 2 ± 3 vs 18 ± 9 mmHg/L/min*). Endogenous ANP activation was greater in the UK dogs (Δ 738 ± 63 vs 394 ± 89 pg/ml*) together with the suppression of aldosterone (Δ 2 ± 2 vs 30 ± 8 pg/dl*). The onset of sodium retention was delayed and at 4 weeks daily sodium excretion was improved (Δ −17 ± 9 vs −35 ± 4 mEq/day*) with increased RBF (218 ± 19 vs 118 ± 20 ml/min*) and less increase in renal vascular resistance (0.33 ± 0.03 vs 0.77 ± 0.2*) without changes in GFR. The increases in LVM in untreated CHF (5.0 ± 0.2 gm/kg) was abolished with treatment with UK (4.0 ± 0.1 gm/kg*) (* = $p < 0.05$). In experimental CHF, pharmacological potentiation of the NPS with inhibition of the RAAS resulted in a delay in the onset and magnitude of sodium retention via tubular mechanisms, reduced systemic and renal vasoconstriction and abolished increases in LVM. These studies support a potential therapeutic action of NEPI/ACEI in delaying progression to overt CHF.

978-94 Acute Heart Failure: A "Relative Brain Natriuretic Peptide Deficiency State". Functional and Therapeutic Implications

J. Aaron Grantham, Daniel D. Borgeson, Margaret M. Redfield, John C. Burnett, Jr.. *Mayo Clinic Rochester, MN*

The natriuretic peptide system, which includes ANP and BNP, mediates potent vasodilatory and natriuretic actions via cGMP. ANP and BNP release is differentially regulated *in vitro. In vivo* BNP is more natriuretic than ANP. The present study tested the hypothesis that in acute heart failure (AHF), plasma BNP is not increased despite increased atrial pressure. Secondly, we determined the functional significance of "BNP deficiency" by administering exogenous BNP in AHF to test the hypothesis that pathophysiologic concentrations result in natriuresis and reduced cardiac filling pressures. Two groups of dogs, control (N = 6) and BNP (N = 6), underwent tachypacing-induced AHF. Cardiorenal and endocrine parameters were analyzed at baseline (C1), in AHF (C2), and during BNP (20 ng/kg/min) or saline vehicle infusion (C3). Despite elevations in plasma ANP during AHF (42 ± 14 vs. 315 ± 83 pg/ml, C1 vs. C2, $p < 0.05$) no natriuretic effect was observed (UNaV 30 ± 5 vs. 9 ± 2 meq/min, C1 vs. C2, $p < 0.05$). Unlike ANP, BNP was not elevated by AHF (32 ± 9 vs. 39 ± 15 pg/ml, C1 vs. C2, p = NS) despite increased PCWP (5.4 ± 0.3 vs. 12 ± 4.2 mmHg, C1 vs. C2, $p < 0.05$). In the BNP group, exogenous BNP increased plasma BNP (26 ± 14 vs. 716 ± 123 pg/ml, C1 vs. C3, $p < 0.01$) with associated reductions in PCWP (13.1 ± 1.3 vs. 8.8 + 0.9 mmHg, control vs. BNP, $p < 0.02$) without altering CO or SVR. Elevated circulating BNP produced natriuresis (UNaV 20 ± 6 vs. 121 ± 44 meq/min, control vs. BNP, $p < 0.05$) associated with elevations in plasma cGMP (17 ± 4 vs. 65 + 7 pg/ml, control vs. BNP, $p < 0.01$) by reducing distal tubular fractional reabsorption of sodium (DFRNa 98.3 ± 0.4 vs. 93.9 ± 2.1%, control vs. BNP, $p < 0.05$) with no change in GFR. We conclude that ANP and BNP release is differentially regulated in AHF resulting in a state of "relative BNP deficiency". That administration of BNP results in natriuresis by renal tubular actions, and results in reductions in cardiac filling pressures. This demonstrates the biologic significance of "BNP deficiency" in AHF and suggests a therapeutic role for BNP administration in AHF.

TUESDAY, POSTER